REMARKS

I. Preliminary Remarks

The Examiner objected to the specification because the ATCC deposit information at pages 14, 177 and 179 were left blank. The foregoing amendments insert the omitted ATCC accession numbers at pages 177 and 178, and adds deposit information relating to IL-17 like polypeptide (IL-17E) at pages 14 and 159. Addition of information designating the depository, accession number and date of deposit is not considered to be new matter added to the application because the deposited material was specifically identified in the application as filed. *See In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985). The additional amendments to the specification correct typographical errors and do not add new matter to the application.

The Examiner objected to claims 1-3 for encompassing non-elected subject matter. These claims have been canceled without prejudice. The dependent claims have been amended to depend from new claim 79. The Examiner also objected to claim 11 as being in improper dependent claim format. Claim 11 has been canceled without prejudice. In light of the foregoing amendment, the Applicants request that all objections to the specification and the claims be withdrawn.

New claim 79 is directed to polynucleotides of the present invention. This claim is supported throughout the specification and does not add new matter. The coding region of SEQ ID NO: 1, which spans nucleotides 159-641, is defined in the sequence listing. Thus, element (b) of claim 79 is supported in the application as filed. The signal sequence of SEQ ID NO: 2 spans residues 1-16 as defined by the underlined sequence in Figure 1 (see page 15, lines 24-28). The Applicants contemplate polypeptides that lack a signal sequence at page 22, lines 15-20, and polypeptides that lack a carboxy terminus at page 22, lines 18-20. Therefore, element (d) of claim 79 is supported in the specification. Elements (a) and (d) of claim 79 also are supported by the specification as one of skill in the art would understand that the mature protein, contemplated at page 11, lines 15-17, and page 28, lines 13-15, would consist of amino acids 17-161 (claim 79, element (d)) of SEQ ID NO: 2, which is encoded by nucleotides 207-641 (claim 79, element (a)) of SEQ ID NO: 1.

Biologically active fragments, as recited in element (e) of claim 79, are supported at page 9, lines 26-31, and page 11, lines 15-17. Polypeptide fragments of amino

acids 17-161 of SEQ ID NO: 2, are supported in the specification at page 32, lines 14-18. Polynucleotides that hybridize under highly stringent conditions are supported at page 32, line 20, through page 33, line 26. Polypeptides that are 90% identical to SEQ ID NO: 2 are supported at page 36, lines 18-23. The biological activity of increasing eosinophils is supported at page 111, lines 19-22 and page 165, lines 3-9.

II. The Present Claims are Entitled to the Priority Benefit of U.S.S.N. 60/213,125

The Examiner asserted that claims 1-8, 10, 11 and 57-59 are not entitled to the benefit of the filing date of U.S. provisional patent application number 60/213,125 (denoted herein as the '125 application). In particular, the Examiner asserted that the disclosure in the '125 application does not provide a credible, specific and substantial utility for the claimed IL-17 like polypeptides and does not enable the subject matter of the pending claims. In response, the Applicants traverse.

The disclosure in the '125 application states that the IL-17 like polynucleotides and polypeptides of the present invention are useful for the treatment or diagnosis of immune disorders and are useful for inhibiting T cell proliferation, T cell activation, B cell proliferation and Ig secretion (page 95, line 16 through page 96, line 9 of the '125 application). The Applicants also contemplate that the IL-17 like polypeptide would be useful for modulating hematopoietic cell growth and for stimulating hematopoiesis, *e.g.*, by stimulating bone marrow and spleen cellularity and increasing eosinophil numbers (page 99, lines 19-22 of the '125 application). Further, the '125 specification states that the IL-17 polypeptide, or antagonists thereof, may be useful in treating or diagnosing tumors such as lymphoma, acute myelogenous lymphoma, chromic myelogenous lymphoma, leukemia and multiple myeloma tumors (page 98, lines 25-29 of the '125 application). Therefore the '125 specification expressly provides a patentable utility in the form of proteins encoded by the DNA sequences of SEQ ID NO: 1, 3 or 9 that are useful for stimulating hematopoiesis and, more particularly, for the production of eosinophils. These utilities are specific, substantial and credible utilities.

Increasing eosinophil number is a "specific and substantial" utility because eosinophils are an integral component of the immune response to infectious organisms. It was well known in the art at the time of filing the '125 application that eosinophils are vital components of an effective immune response against bacterial and parasitic infection. In

support of this position, provided herewith is an excerpt from D. Zucker Franklin *et al.*, *"Atlas of Blood Cell - Function and Pathology"* Ed. Ermes s.r.l. Milan, Italy/Lea & Febiger, Philadelphia, PA USA, p. 268 (1998) (attached as Appendix A). In brief, it was known that eosinophils "phagocytize bacteria, particles, sensitized erythrocytes . . . and other antigen/antibody complexes." (Franklin *et al.*, p.269, col. 1). Eosinophils also "respond to chemotaxis by products released from bacteria and components of the complement system," as well as "kill microorganisms and parasites." (Franklin *et al.*, p.269, col. 1). Furthermore, "[e]osinophils also neutralize histamine . . . and they elaborate a substance called eosinophil derived inhibitor . . . which is purported to inhibit mast cell degeneration." (Franklin *et al.*, p.269, col. 2). The treatise goes on to state that "[t]herefore, eosinophils are likely to play an important, if not critical role in abrogating the immediate hypersensitivity response." (Franklin *et al.*, p.269, col 2).

Applicants note that the disclosure of the invention provided in the first provisional patent application was confirmed by Examples 1-7 of the second provisional application (U.S.S.N. 60/266,159; denoted herein as the '159 application). For example, transgenic mice that overexpress IL-17E are described in the '159 application. Hematological analyses of these mice revealed an increase in total leukocytes, neutrophils, lymphocytes and eosinophils as compared to non-transgenic mice (page 150, line 10, through page 151, line 2, of the '159 application). The histopathological analyses of these mice showed a marked increase in mesenteric lymphadenopathy, splenic lymphoid hyperplasia, red pulp eosinophilic hyperplasia and bone marrow eosinophilic hyperplasia (page 154, lines 9-14 of the '159 application). The' 159 application expressly contemplated that the IL-17 like polypeptide of the present invention plays a role in inflammation and myelopoiesis, particularly in the development of eosinophils and B-lymphocytes (page 155, lines 23-27, of the '159 application).

Furthermore, the data provided in the present application confirms that the utility of the IL-17 like polypeptide in stimulating hematopoiesis and increasing eosinophil numbers, as originally disclosed in U.S.S.N. 60/213,125. The '125 specification asserts that IL-17 like polypeptide may stimulate T-cell proliferation, hematopoiesis and cellularity of the bone marrow as well as increase the number of eosinophils. Table 5, at page 182 of the application, demonstrates that mice overexpressing IL-17 like polypeptide exhibited a significant increase in CD5+CD19+ lymphocytes and CD34+CD19+ lymphocytes in the

lymph node. The mice also exhibited a significant increase in CD4+ eosinophils in the bone marrow.

The '125 specification also states that the polypeptide of the present invention, and antagonists therefor, are useful for the treatment or diagnosis of immune disorders. The experiments described in the specification demonstrate that IL-17 like polypeptide induced human T-lymphoblasts to release the proinflammatory cytokines TNF-α, IL-1α and IL-6 (see page 180-181 of the '125 application). As IL-17 cytokines are generally known to induce expression of proinflammatory cytokines (reviewed in Mosley *et al., Cytokine & Growth Factor* Reviews, 14: 155-174, 2003), these data substantiate the assertion in '125 that the IL-17 like polypeptide is a IL-17 cytokine family member and confirm its expected utility in preventing and treating immune disorders.

In response to the asserted lack of enabling support in the '125 application for the pending claims, the Applicants submit that the '125 specification provides ample description of DNA and protein sequences, expression vectors, host cells, culture systems, purification methods, pharmaceutical formulations and therapeutic administration. Moreover, the Examiner effectively argued that one cannot enable a non-existent use ("the utility/enablement requirement of 35 U.S.C. §101/112, first paragraph"; Office Action at page 3), and the preceeding remarks have established that such a position is flawed by a defective predicate in that U.S.S.N. 60/213,125 expressly disclosed a number of patentable utilities for the presently claimed subject matter. Therefore, the specification enables one of skill in the art to make and use the claimed subject matter.

The disclosure in the '125 application, from which priority is claimed in the present application, asserts credible, specific and substantial utilities for the presently claimed subject matter. The credibility of this asserted utility is confirmed by the experimental evidence provided in the present application. Therefore, the present application is entitled to the effective filing date of June 22, 2000. The Applicants request that the Examiner clarify the record by expressly withdrawing the statement that the present application is not entitled to the benefit of the earliest claimed priority date.

III. The Rejection under 35 U.S.C § 112, Second Paragraph, Should be Withdrawn

The Examiner rejected claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 112, second paragraph, as assertedly indefinite for omitting essential elements or for reciting

percent identities in the alterative. In response, the Applicants submit that the rejection has been rendered moot by the foregoing amendments.

Claims 1-3 were assertedly indefinite as these claims were directed to polynucleotide molecules that hybridize under moderate or stringent conditions to the polynucleotide sequence of the present invention. Claims 1-3 were canceled without prejudice and the rejection is thereby rendered moot. However, new claim 79 is directed to a polynucleotide molecule that hybridizes under highly stringent conditions to the nucleic acid sequence of SEQ ID NO: 1. The hybridization conditions are clearly defined in new claim 79 and the recited hybridization conditions are supported at page 33, line 16-20.

Claim 2 was also determined to be indefinite for reciting "at least about 70, 75, . . . 99% identical" to the polynucleotide sequences of the present invention. Claim 2 has been canceled without prejudice and therefore the rejection has been rendered moot. New claim 79 is directed to a polynucleotide that encodes a polypeptide that is at least 90% identical to SEQ ID NO: 2. This claim does not recite percent identities in the alternative in compliance with 35 U.S.C. § 112, second paragraph and therefore distinctly points out the claimed invention.

In view of the foregoing amendments and remarks, the Applicants submit that the rejection of claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 112, second paragraph, for indefiniteness has been rendered moot and should be withdrawn. A rejection of new claim 79 on the same grounds would be improper.

IV. The Rejection under 35 U.S.C. § 112, First Paragraph Should be Withdrawn

A. Enablement

The Examiner rejected claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 112, first paragraph, for lack of enablement. In particular, the Examiner stated that the specification does not reasonably provide enablement for various variants and fragments of SEQ ID NO: 1 or for a nucleic acid encoding SEQ ID NO: 2. Claims 1-3 have been canceled without prejudice. The foregoing amendment adds new claim 79 which incorporates subject matter of the canceled claims. The Applicants traverse this rejection as it may be applied to new claim 79.

The Applicants submit that new claim 79 should not be rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. This claim is directed to a polynucleotide that comprises a nucleic acid sequence that encodes a polypeptide that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2. One of skill in the art can use the disclosed polynucleotide sequences to identify sequences that are 90% identical to SEQ ID NO: 1. In particular, Example 1 teaches how to identify polynucleotides encoding polypeptides related to the IL-17 like polypeptides using EST probes to screen cDNA libraries. (See specification pages 157-159.) Therefore, the starting materials are taught in the specification and the methods to identify and make the variant sequences, such as synthesizing polynucleotides and amplification of native polynucleotides, are conventional in the art. In addition, the specification identified a variety of commercially available computer programs that will assess nucleotide sequence similarity to SEQ ID NO: 2, such as GAP, BLASTP and FASTA. (See specification, pages 52-55.) New claim 79 also encompasses polynucleotides that encode biologically active fragments of a polypeptide comprising the sequence of SEQ ID NO: 2, and the specification teaches how to make biologically active fragments at page 22, line 15, through page 23, line 12.

The specification also guides one of skill in the art in identifying which nucleotides can be altered within a polynucleotide sequence while the encoded polypeptide retains the required biological activity. (See specification page 37, line 14, through page 47, line 16.) Assays for determining the required biological activity of the polypeptides encoded by the claimed polynucleotide variants are conventional and are taught in the specification. In particular, Example 4 (pp. 162-170) provides methods for measuring eosinophil number using histological methods and Examples 5 (pp. 170-177) and 10 (pp. 181-183) provide methods for measuring eosinophils using FACS analysis.

New claim 79 is also directed to polynucleotides that comprise a nucleic acid sequence that hybridizes to the complement of SEQ ID NO: 1 under highly stringent conditions. Techniques for identifying nucleic acids that hybridize under stringent conditions are well known in the art. The specification defines stringent hybridization conditions (specification, page 33, lines 16-20), provides methods for carrying out the hybridization reactions (specification, page 33, line 11, through page 34, line 30), and cites several references establishing that the techniques are well known in the art, *e.g.*, Sambrook, *et al.* and Anderson *et al.*

In view of the foregoing remarks, the Applicants submit that a rejection of new claim 79 under 35 U.S.C. § 112, first paragraph, for lack of enablement would be improper. Claims 4-8, 10, 12 , 57-59 directly or indirectly depend from new claim 79. In view of the forgoing amendment and remarks, the rejection of the dependent claims for lack of enablement should be withdrawn.

B. Written Description

The Examiner rejected claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 112, first paragraph, for failing to provide a written description of the claimed subject matter. Specifically, the Examiner asserted that the claims are drawn to various variants of SEQ ID NO: 1 that are not described in the specification in such a way as to reasonably convey to one of skill in the art that the Applicants were in possession of the claimed invention at the time of filing. Claims 1-3 have been canceled without prejudice. The foregoing amendment adds new claim 79. The Applicants traverse this rejection as it applies to new claim 79.

New claim 79 is directed to polynucleotides which encode polypeptides that are at least 90% identical to SEQ ID NO: 2, and that have the capacity to increase eosinophil number. The structural and functional limitations recited in new claim 79 meets the Written Description Guidelines of the United States Patent and Trademark Office, 66 Fed. Reg. 1099 (January 30, 2001). In particular, Example 14 of the Revised Interim Written Description Guidelines Training Materials remains consistent with those guidelines and teaches that a claimed variant polynucleotide that is substantially similar to a sequence taught in the specification, along with a functional limitation that the claimed variant polynucleotide encodes variant polypeptides that exhibit an identified activity, meets the written description requirement if the required activity can be determined as described in the specification. In the instant case, the claimed polynucleotide must encode a polypeptide having a sequence that is at least 90% identical to SEQ ID NO: 2, and therefore do not have substantial variation from the sequence of SEQ ID NO: 2, as taught in the specification.

New claim 79 is also directed to polynucleotides that encode polypeptide fragments of SEQ ID NO: 2 that retain the capacity to increase eosinophil number. Active fragments of the amino acid sequences of the present invention are contemplated in the specification at page 9, lines 26-29, and page 22, line 15, through page 23, line 12. The claimed fragments are structurally defined as these fragments are limited to specific residues

of SEQ ID NO: 1. In addition, the recited fragments are functionally defined as those that retain the capacity to increase eosinophil number. Therefore, one of skill in the art would have recognized that the number of fragments encompassed by claim 79 is not infinite, that a small fragment (*e.g.* 2 or 3 residues) will not retain the required function, and importantly, that the Applicants were in possession of the functional fragments embraced by the claim.

Finally, the stringent hybridization conditions recited in new claim 79 was explicitly supported in the specification at page 33, lines 15-20. Accordingly, the structural and functional limitations of claim 79 are described in the specification in such a way as to convey to one of skill in the art that the Applicants had possession of the claimed invention as of the effective filing date of the application.

In view of the foregoing remarks, the Applicants submit that the rejection of new claim 79 under 35 U.S.C. § 112, first paragraph, for lack of written description would be improper. Claims 4-8, 10, 12 , 57-59 directly or indirectly depend from new claim 79. In view of the forgoing amendment and remarks, the rejection of the dependent claims for lack of written description should be withdrawn.

V. The rejection under 35 U.S.C. §102 should be withdrawn.

A. Marra *et al.*

The Examiner rejected claims 1-5, 7, 11 and 57 under 35 U.S.C. § 102(b) as assertedly anticipated by Marra *et al.*, locus W88186 (12 September 1996). In particular, Marra *et al.*, was characterized as disclosing a sequence with 100% identity to nucleotides 609-631 of SEQ ID NO: 1. Claims 1-3 were canceled without prejudice. New claim 79 was added. The Applicants submit that a rejection of claim 79 under 35 U.S.C. § 102(b) would be improper.

New claim 79, elements (a) - (d) recite polynucleotides that comprise nucleotide sequences that are not identical to the sequence disclosed in Marra *et al.* In addition, the polynucleotide sequences recited in elements (e) - (g) of claim 79 encode polypeptide fragments or variants that retain the capacity to increase eosinophil number. Marra *et al.*, fails to disclose, expressly or inherently, any polynucleotide encoding a polypeptide that increases eosinophil number.

Claims 4-5, 7, 11 and 57 depend directly or indirectly from new claim 79. Thus, in view of the foregoing amendment, the claims are not anticipated by Marra *et al.*, and the rejection under 35 U.S.C. § 102 (b) should be withdrawn.

B. Gorman *et al.*, WO 200042187

The Examiner rejected claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 102(a) as assertedly anticipated by Gorman *et al.*, WO 20024218. The Examiner asserted that Gorman *et al.*, disclosed a nucleotide sequence that is 99.8% identical to nucleotides 140-664 of SEQ ID NO: 1 and that encodes an amino acid sequence that is 100% identical to SEQ ID NO: 2. In response, the Applicants traverse.

The remarks provided above demonstrate that the present application is entitled to an effective filing date of June 22, 2000 (the filing date of provisional patent application U.S.S.N. 60/213,125. Gorman *et al.*, was published July 20, 2000 and therefore, is not available as prior art against any of the pending claims. Thus, the claims are not anticipated by Gorman *et al.*, and the rejection of claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 102(a) over Gorman *et al.*, should be withdrawn.

VI. The rejection under 35 U.S.C. § 101 for double patenting should be withdrawn.

The Examiner provisionally rejected claims 1-8, 10, 11 and 57-59 under 35 U.S.C. § 101 for statutory double patenting in view of the claims of U.S. patent application no. 09/886,404. The '404 application is no longer a pending application and the Applicants have received a Notice of Abandonment. Therefore, the Applicants respectfully request that the provisional rejection be withdrawn.

CONCLUSION

In view of the amendments and remarks made herein, claims 4-8, 10, 57-58 and 79 are in condition for allowance and the applicants request notification of same.

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Respectfully submitted,

By _____
Sharon M. Sintich
Registration No.: 48,484
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Agent for Applicant